## REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claim 6 is currently being amended.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims as set forth above, claims 6-7 and 12-14 are now pending in this application.

### I. REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Applicants disagree with the rejection under § 112, first paragraph, for alleged lack of "possession" of the claimed "enzyme." To further prosecution, the aqueous extract of claim 6 has been limited to an extract obtained using a mixture of amylase and protease. The Office has acknowledged that such a mixture is fully described and exemplified in the application (Office Action, p. 5, ll. 7-8).

Accordingly, Applicants respectfully request that this objection be withdrawn.

### II. REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The Office rejected claim 6 (and its dependent claims 7 and 12-14) as improperly depending from non-elected claim 1. Applicants have obviated this ground of rejection by rewriting claim 6 in independent form, inserting the method of preparation of the aqueous peptide extract from claim 1.

### III. REJECTIONS UNDER 35 U.S.C. §§ 102(B) AND 103(A)

The Office has rejected claims 6-7 and 12-14 under 35 U.S.C. §§ 102(b) and 103(a) over JP 2003-155213.

Applicants respectfully traverse. The invention provides a fully hydrosoluble peptide extract of maca for convenient use in cosmetic products. Since raw maca (dehydrated powder) is almost insoluble in water, its use in cosmetic care products is difficult to consider as such (see specification, p. 4, ll. 4-6 and p. 3, ll. 35-37). On the contrary, the maca extract disclosed in JP 2003-155213 is not hydrosoluble since it is used as a substantially moisture-free powder or an oily liquid (see claims).

Present claim 6 is directed to an aqueous peptide extract of maca, obtained by a particular method of preparation. The use of this particular method results in the following special distinguishable features of the obtained maca extract:

- it is fully hydrosoluble,
- it contains small, hydrolyzed peptides,
- it also contains hydrolyzed sugars, in particular hydrolyzed starch.

JP 2003-155213 does not disclose such a maca extract. Indeed, the maca extract described in JP 2003-155213 can be clearly distinguished from the extract according to the present invention as follows:

- the JP 2003-155213 maca extract is not hydrosoluble and is even water-sensitive (see claims, and page 11 lines 1-3: "Because humidity reduces the proteolytic activity of papain, each component of the face-washes was a substantially moisture-free powder or an oily liquid");
- the JP 2003-155213 maca extract does not contain the low molecular weight hydrolyzed peptides of the extract according to the present invention; and
- the JP 2003-155213 maca extract lacks hydrolyzed sugars

**A. The JP 2003-155213 maca extract is not hydrosoluble**

The maca extract of JP 2003-155213 is not hydrosoluble despite the use of papain, because the disclosed process fails to hydrolyze the protein portion of the maca extract.

JP 2003-155213 discloses the following process (see English translation, p. 9, first paragraph):

- Preparation of an aqueous solution containing 50% wt of papain,
- Spraying of this solution onto the maca powder so that the weight of sprayed solution onto the powder is 3.0% by weight based on the weight of the powder,
- Mixing for one hour of the sprayed maca powder,
- Drying the mixed powder by heating at 40°C followed by blowing with air.

**B. The JP 2003-155213 maca extract lacks small hydrolyzed peptides**

JP 2003-155213 nowhere discloses that any proteins have been hydrolysed. As explained below, a skilled artisan would conclude that no protein hydrolysis occurred during the reaction disclosed in JP 2003-155213, based on the insufficient amount of water, on the sub-optimal reaction temperature, and on the fact that JP 2003-155213 itself indicates that no papain activity is detected at the end of the reaction,.

The protease activity of papain requires water to hydrolyse proteins into peptides. This is clear from the definition of "hydrolysis" from Merriam-Webster Online Dictionary (submitted herewith), which implies that each peptide bond breaking by hydrolysis needs a corresponding water molecule.

In particular, peptide bond hydrolysis is an equilibrium reaction, and proteases such as papain have been shown to catalyze both peptide bond hydrolysis and the reverse reaction of peptide bond synthesis, depending on the reaction conditions (see Bergmann et al., p. 708, ll. 2-10 from bottom, submitted herewith). Furthermore, the amount of water present in the reaction medium influences the reaction equilibrium, and decreasing the amount of water favors the reverse peptide synthesis reaction while simultaneously decreasing hydrolysis efficiency (see WO 03/064669, submitted herewith, in which papain is used in a low-water-content medium to synthesize Nα-acyl-L-arginine esters by reverse hydrolysis).

In JP 2003-155213, the total amount of water (residual water of maca extract + water of the sprayed solution) during the alleged hydrolysis step is only of approximately 10% by weight. Such a low amount of water is clearly insufficient to permit papain to hydrolyse proteins into peptides.

Indeed, in view of the very low amount of water present during the reaction described in JP 2003-155213, it is clear that residual protease activity of papain should be very low, too low to obtain low molecular weight water-soluble peptides as in the extract according to the present invention.

This is further supported by comparing the properties of papain itself, for which optimum temperature for activity is 65°C (see Sigma-Aldrich document relating to papain, p. 1, l. 17, submitted herewith), with the reaction conditions used in JP 2003-155213.

In JP 2003-155213, the mixing and reaction step are conducted at room temperature (a temperature of 40°C is only used to dry the mixture). One shall assume that the sought reaction was done before this step, at room temperature in the absence of further precision.

Therefore, in this process disclosed in JP 2003-155213, the temperature is significantly lower than the optimum temperature for activity. Accordingly, during these steps disclosed in JP 2003-155213, papain cannot hydrolyse the proteins of maca. This is another confirmation that in the method used in JP 2003-155213, it is very doubtful that any protease activity at all can be performed and thus lead to the hydrolysis of maca proteins.

Moreover, JP 2003-155213 indicates that the proteolytic activity of maca powder after the treatment is undetectable, which according to JP 2003-155213 means that no papain remains in the powder. Since there is no purification step for removing papain, this may only be interpreted as meaning that papain is not anymore active. However, an enzyme is normally denatured by a heating process or with a protease inhibition solution.

In conditions suitable for a protease enzyme, i.e. when proteins and water are both present and no denaturating step has been performed, a protease will be active until all the

proteins and peptides have been hydrolysed into amino acids. At the end of the process (without denaturating step), the enzyme normally still shows a proteolytic activity.

The only conclusion that may be drawn from the fact that no papain activity is detected at the end of the reaction in JP 2003-155213 is that, as explained above, the reaction conditions are not suitable for papain to display any protease hydrolysis activity, even at the beginning of the reaction.

Based on the insufficient amount of water, on the sub-optimal reaction temperature, and on the fact that JP 2003-155213 itself indicates that no papain activity is detected at the end of the reaction, it is thus very doubtful that any protein hydrolysis at all may have occurred during the reaction.

In any case, even if some degree of protein hydrolysis may have occurred, it is clearly not sufficient to lead to the production of small peptides that may be purified by ultrafiltration, which only retains low molecular weight compounds.

Thus, the extract of JP 2003-155213 does not contain the low molecular weight hydrolyzed peptides of the extract according to the present invention.

### C. The JP 2003-155213 lacks hydrolyzed sugars

Finally, the extract of JP 2003-155213 also does not contain the same hydrolyzed sugars, in particular hydrolyzed starch, that are present in the extract according to the invention.

Indeed, no amylase is present in the reaction medium used in the method described in JP 2003-155213, so that only non-hydrolyzed starch may be present in the extract of JP 2003-155213, while the extract according to the invention further comprises hydrolyzed sugars.

This is clearly confirmed in JP 2003-155213, which indicates that the maca extract after papain treatment comprises hardly-soluble or insoluble substrates such as polysaccharides and fiber originally contained in the axial root and the hypocotyl segment in the raw maca (see page 10 lines 14-16 of the English translation provided to the Examiner).

To conclude, the extract of maca obtained using the method described in JP 2003-155213 is quite different from the aqueous extract comprising small peptides and sugars according to the invention. JP 2003-155213 thus fails to satisfy all the limitations of claim 6. Applicants request that the Office withdraw the rejection under § 102(b) over JP 2003-155213.

### D. The claimed invention is nonobvious

In addition, the claimed invention is nonobvious over JP 2003-155213. The claimed aqueous peptide extract provides unexpected results since the peptide extract of maca obtained in the invention permits to stimulate the cell metabolism from dermal fibroblasts (see Example 2-1), in particular of "aged" fibroblasts, thus opposing intrinsic skin ageing (see Example 2-2). Moreover, the claimed peptide also prevents the formation of free radicals (see Example 2-3). The art of record fails to suggest any such activity.

The same arguments apply for all the other claims, and the Applicants thus estimate that all pending claims are new and inventive over the prior art.

## IV. REJOINDER

Upon allowance of claim 6, Applicants request rejoinder of method of making claims 1-5 and 8, solid peptide extract claims 9-11, method of use claims 15-16, 17-22, 24-33, and cosmetic composition claim 23, each of which contains all the limitations of claim 6.

## CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or

even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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